6450-01-P

DEPARTMENT OF ENERGY

Record of Decision to Withdraw from Production and Distribution of the Radioisotope Germanium-68 Used for Calibration Sources

AGENCY: Office of Science, Department of Energy.

ACTION: Record of Decision.

SUMMARY: The Department of Energy (Department or DOE) Isotope Program, within the Office of Science, currently produces and distributes the radioisotope germanium-68 (Ge-68). There are two primary uses of the Ge-68: in the manufacture of calibration sources for Positron Emission Tomography (PET) scanners used for diagnostic medical imaging; and in the manufacture of germanium-68/gallium-68 (Ge-68/Ga-68) generators, which provide Ga-68 as a positron source in radiopharmaceuticals used in PET imaging.

The Department published a Notice of Inquiry and Request for comment in the **Federal Register,** on March 8, 2013, concerning its consideration of withdrawal from commercial production of Ge-68. The Department received numerous comments in response to this Notice of Inquiry, evaluated substantial information provided by one private domestic company seeking the Department's withdrawal, and assessed other available information. The Department determined that Ge-68 is reasonably available from the commercial sector for use in the manufacture of calibration sources but not for use in Ge-68/Ga-68 generators. The Department published a Notice of Intent and Request for comment in the **Federal Register**, on April 9, 2014, to provide the public with notice

and seek public comment on the Department's intent to withdraw from the production and distribution of Ge-68 used in the manufacture of calibration sources, while maintaining its current position in the production and distribution of Ge-68 for Ge-68/Ga-68 generators. Three comments in response to this Notice of Intent were received and assessed by the Department to conclude the evaluation process with this Record of Decision. The Department's decision is to: (1) withdraw from sales of Ge-68 for the purpose of fabricating calibration sources, while maintaining production capability in the event circumstances change; (2) maintain its current position in the production and distribution of Ge-68 for use in the manufacture of Ge-68/Ga-68 generators; and (3) require the Department's Ge-68 customers to sign an end-use statement that the Ge-68 will be used only in the fabrication of Ge-68/Ga-68 generators.

FOR FURTHER INFORMATION CONTACT: Dr. Marc Garland, Program Manager, Office of Nuclear Physics, Office of Science, U.S. Department of Energy, Germantown Building, SC-26.2, 1000 Independence Ave., SW, Washington, DC 20585, Tel: 301-903-9576.

SUPPLEMENTARY INFORMATION:

It is the Department's policy to refrain from competition with private industry in the commercial production and distribution of radioisotopes when those radioisotopes are reasonably available commercially. This policy was announced in the **Federal Register** notice, 30 FR 3247 (March 9, 1965), entitled "Policies and Procedures for Transfer of Commercial Radioisotope Production and Distribution to Private Industry" ("Statement of Policy"). The

Statement of Policy provides criteria and guidance on withdrawal from the market and states that when the Department determines to voluntarily withdraw from the commercial production and distribution of particular radioisotopes, it will publish a notice of such intent for public comment.

Background

The Department currently produces and distributes the radioisotope Ge-68. The Department was made aware of domestic private industry development of commercial production and distribution of this radioisotope in the United States, in addition to the distribution in the United States of the radioisotope produced by foreign entities. In light of these circumstances, a Notice of Inquiry and Request for comment entitled "Consideration of Withdrawal from Commercial Production and Distribution of the Radioisotope Germanium-68" ("Notice of Inquiry") was published in the **Federal Register**, 78 FR 15009 (March 8, 2013), announcing the Department's intent to conduct an evaluation and to request comments and information from the public for consideration in the evaluation.

The Department received numerous comments in response to the Notice of Inquiry from private citizens affected by the use of Ge-68 in Ge-68/Ga-68 generators critical in medical imaging for certain cancers, and from some private companies involved in the manufacture of products for medical purposes. The Department conducted an evaluation of all available information, including all comments received in response to the Notice of Inquiry, and subsequently published a Notice of Intent to Withdraw from Production and Distribution of the Radioisotope Germanium-68 Used for

Calibration Sources ("Notice of Intent and Request for Comment") ("NOI") in the **Federal Register**, 79 FR 19610 (April 9, 2014). The NOI announced the Department's intent to withdraw from production of Ge-68 for the manufacture of calibration sources, but to maintain production and distribution of Ge-68 for Ge-68/Ga-68 generators. To provide assurance of supply of Ge-68 for calibration source purposes, the Department announced that it would maintain production capability but not engage in sales to the marketplace. Sales of Ge-68 for calibration sources would end by April 30, 2014, and thereafter customers would be required to sign an end-use statement that the Ge-68 would be used in the fabrication of Ge-68/Ga-68 generators. The NOI presented the basis for the Department's proposed actions and solicited comments regarding those actions.

Evaluation and Determination

The Department received three comments in response to the NOI, two from the general public and one from private industry. The responses from the general public were received from a university researcher involved in Ga-68 radiopharmaceutical development and a cancer patient who benefits from the use of Ga-68 radiopharmaceuticals; both responses were in support of the Department's announced intent to maintain production for use in Ge-68/Ga-68 generators. Neither commenter objected to the Department's withdrawal from the production and distribution of Ge-68 used in calibration sources.

The response received from private industry, Mallinckrodt Pharmaceuticals, supported the Department's announced intent to withdraw from production of Ge-68 for the manufacture of calibration sources, but provided additional information and requested the Department reconsider

the announced intent to maintain production and distribution of Ge-68 for Ge-68/Ga-68 generators. In summary, Mallinckrodt requested reconsideration on the bases that its Ge-68 is qualified for use in Ge-68 generators, and that there is effective competition in the market for the supply of Ge-68 for generators.

Mallinckrodt provided information indicating that it's Ge-68 is now qualified for use in Ge-68/Ga-68 generators, in response to the Department's concern expressed in the NOI regarding the lack of domestic producers of Ge-68 qualified for use in Ge-68/Ga-68 generators. The Department acknowledges that Mallinckrodt is now a domestic producer of Ge-68 qualified for use in Ge-68/Ga-68 generators.

In regard to effective competition, Mallinckrodt provided information identifying as major Ge-68 suppliers Brookhaven National Laboratory (BNL), Los Alamos National Laboratory (LANL) (United States), Cyclotron Co. Ltd. {Obninsk, Russia), and iThemba Laboratories/NAC (Faure, South Africa), and requested these suppliers be considered as constituting effective competition in the supply of Ge-68. In the NOI, the Department had stated that, in the absence of a Department supply of Ge-68 for the manufacture of generators, Mallinckrodt would be the sole domestic source of Ge-68 for generators, that a single domestic supplier could be problematic for the U.S. market for generators, and that the Department's continued participation in that segment of the market as a second domestic supplier would serve to reduce the potential for impediments to research and development leading to FDA approval of Ga-68 radiopharmaceuticals. The United States suppliers identified by Mallinckrodt- BNL and LANL – are both Department of Energy production sites, so if the Department exited the Ge-68 market, Mallinckrodt would be the sole domestic supplier of Ge-68. Mallinckrodt correctly noted that the Department's policy on withdrawal from radioisotope

production and distribution may include consideration of foreign producers to evaluate effective competition in the market. Even with two potential foreign sources of supply, however, the Department concluded that insufficient data, and thereby inadequate evidence, exists on the capability of these suppliers to provide an adequate supply and effective competition in the market to justify the Department's withdrawal. Use of Ge-68 in Ge-68/Ga-68 generators, which provide Ga-68 as a positron source in radiopharmaceuticals used in PET imaging, is a relatively new, unique and evolving application of this isotope in a critical state of development for cancer research. In consideration of the additional information provided on potential suppliers balanced against public comments and the critical need and use of Ge-68 in the context of Ge-68/Ga-68 generators, the Department affirms its initial conclusion that a sole domestic supplier and the uncertain contribution of foreign suppliers would not represent effective competition in the supply of Ge-68 in support of the Nation's significant interest in the research and development of Ga-68 radiopharmaceuticals.

The Department also affirms its intent that, to help provide assurance of supply of Ge-68 for calibration source purposes, DOE will maintain production capability, but not engage in sales to the marketplace, such that production would resume in a timely manner if Mallinckrodt and other suppliers are not be able to adequately serve the market or if private supplier pricing substantially increases and has a negative impact on the development and utilization of Ge-68 products.

To serve the Nation's interests in the advancement of health care, the Department will continue to produce and distribute Ge-68 for use in the manufacture of Ge-68/Ga-68 generators until such time as firm data exists establishing that there are multiple domestic suppliers capable of fully satisfying the needs of the United States market without the participation of Department in that market.

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